

William Little Foundation

Text of speeches made on 21st September 2016 by Trustees Kasper de Graaf and Prof Michael Crawford at a House of Lords event to mark the 25th anniversary of The Little Foundation



Kasper de Graaf

Those of you with an eye for detail may have spotted that 1990 – the year this charity was established – is actually 26, not 25, years ago.

However, the trustees in their wisdom have decided that just because we did not mark our quarter century on the day, that is no reason to pass up the opportunity to mark it at all.

And there is a reason we have picked tonight as our official 25th birthday. It is that we have reached a point where we can take stock of the work that has been done, and launch a new, funded programme of research, together with a strategy for developing the charity and disseminating the knowledge we acquire.

Before we hear a little later from Professor Crawford about the science, I have been asked to say a few words about how we got here and what we are planning to do.

The Little Foundation was set up in 1990 by Ian Dawson-Shepherd. Dawson-Shepherd by that time had already been in the vanguard of campaigning for people with cerebral palsy for forty years.

The father of a daughter, Rosemary, with severe cerebral palsy, he had joined with three others to form the National Spastics Society in 1952 and became its chairman. Later renamed Scope, our sister organisation has done a huge amount to change attitudes, to support sufferers and their carers, and to empower people with cerebral palsy to overcome the challenges with which they were born.

It has played an important role in the journey of many of the athletes who have won glory in the Paralympics in Rio over the last two weeks and who so fittingly and movingly are described as superhumans, given their incredible achievements in the face of such adversity.

There are others in this room better versed in our early history than I, and it is good to see one of our former Vice-Presidents, the chess grandmaster Raymond Keene, here tonight, as well as one of our current Vice-Presidents, Baroness Nicholson.

We've heard from two other Vice-Presidents who regrettably cannot be with us – Tim Yeo, who is on a business trip to the United States, and Dame Judi Dench, who is filming – but both have sent their best wishes.

I would like at this point to pay tribute to someone else who can't be here this evening.

Christopher Robinson was at Ian Dawson-Shepherd's side from day one. He took over as Chairman of Trustees when Ian passed away in 1996, and provided the continuity that has got us, as Lord Hameed said earlier, to the point where we can see the promised land.

Christopher retired from the board in 2013 and graciously accepted the 'onorific title of President. I spoke to him at the weekend. He described himself as hors de combat, but delighted that we are launching a new programme and he asked me to pass on his warm wishes to everyone gathered here this evening.

I would also like to place on record our gratitude and thanks to the late Lord Walton, the former President of the General Medical Council and of the World Federation of Neurology, our Patron until he died in April of this year.

Ian Dawson-Shepherd was always keen on medical research. As long ago as 1960 he persuaded the Spastics Society to fund a Paediatric Research Unit at Guy's Hospital to look into the causes of cerebral palsy.

The impetus for setting up The Little Foundation thirty years later again came from Rosemary, whose cerebral palsy had inspired his campaign back in 1952, and who herself died in 1986.

Rosemary had said it was wonderful he was helping sufferers, but couldn't he do something to stop babies being born with the condition?

So it was that our organisation was founded in 1990 and named after William John Little, the Victorian neurosurgeon who in the mid-eighteen fifties was the first to identify the condition we now know as cerebral palsy, which for many years was known as Little's Disease.

The Foundation's research focus quickly turned to nutrition and in the mid-1990s, Ian Dawson-Shepherd was raising funds for a project looking into the problems of nutrition and its pre-natal effect on babies.

The Little Foundation was instrumental in formulating and funding the European Cerebral Palsy Study, involving almost 600 children born with cerebral palsy between 1996 and 1999 in England, Scotland, Portugal, Ireland, Sweden, Germany and Finland.

This study concluded that 'obstetric mishap', that is, accidents or errors during childbirth – until then commonly regarded as the major cause of cerebral palsy – could be blamed in

only a small number of cases. If other, pre-birth causes could be established, then this suggested that in many cases, cerebral palsy might be preventable.

Since this work was published, ten years ago, the Foundation has promoted a wider discussion about the causes, including sponsoring over 20 international workshops and a seminar of experts to review the evidence.

In recent years we have collaborated with Imperial College and other institutions to frame and seek funding for further research, and tonight we are ready to launch a new programme for continued research, set out in this report.

I am delighted to welcome AnnieBelle Sassine, a postgraduate researcher at Imperial College, and to announce that the Foundation has committed to fund AnnieBelle's research for the coming year into the correlation between maternal fatty acids and pregnancy outcomes.

We will be raising funds to continue that research thereafter and to undertake further research to specifically evaluate how the mother's nutritional state before conception affects the likelihood of brain abnormalities at birth.

We have also started laying the foundations for more significant fundraising and disseminating the outcomes of the research, building on the excellent efforts of the individuals and companies who have organised activities like quizzes and marathons to raise funds for the charity in recent years, some of whom are here this evening.

Among the donations we have received we are extremely grateful to the late Mr George Lee, who passed away earlier this year and left the Foundation a substantial legacy which is a significant factor in our ability to move our work to the next phase and which demonstrates the power and significance of what individual gifts can do.

The important thing about this charity is the cause and the work we do, but there are a couple of other people I want to thank.

First, Julia Adey, the Secretary to the Trustees, who is currently the second-longest serving official of the Foundation, the fount of such institutional memory as we have, and a magnificent herder of the always busy and sometimes elusive cats who are our trustees.

I also want to express a special thanks to Andrea Mátysz-czyk who has so splendidly organised this evening.

There is one person who has been with this organisation since the beginning – so, even longer than Julia – and who is responsible for our clear focus on nutrition.

Some of you may have heard David Attenborough's programmes *The Waterside Ape* on Radio 4 last week.

I am not going to hazard a David Attenborough impression, but I will quote him.

“Over the last half century,” said the great broadcaster, “one person has probably done more than anyone to establish that the marine food chain was the essential resource for humans as they evolved a big brain.”

We are indeed extraordinarily fortunate that in Professor Michael Crawford, Director of the Institute of Brain Chemistry and Nutrition at Imperial College London, we have one of the world’s biggest brains and leading authorities on this topic as our scientific mentor and guide.

It is the work done by Michael and by his Imperial colleagues Professor Mark Johnson, Dr Enitan Ogundipe, Dr Yiqun Wang and AnnieBelle Sassine, all of whom are here this evening, that offers the prospect of eradicating, or at least seriously reducing, the incidence of cerebral palsy. We thank them for what they have already done and we plan, with your assistance, to do all we can to support this work, because we believe it can help achieve the objectives for which we were established.

I will now leave you to enjoy your dessert and your conversations for a while and then it will be time for you to see that a big brain does not necessarily mean a big head, because Michael, who in a short while will tell you something about the science, will doubtless attempt some self-deprecation to mitigate the more-than-merited build-up I have given him.

Don’t believe a word of it.



Prof Michael Crawford

The reason I am here is to tell you something of the scientific background and research we are doing, which could make cerebral palsy a thing of the past.

In 2010 Josette Sharon then CEO of UN World Food Programme commented in her report to the Board: “We now know more about nutrition. It is not just about providing a full cup for the child; it is what is in the cup that matters”. She went on to say, “If a child under 2 years of age is malnourished, that child will be sentenced to a life of physical and mental limitations”.

The full weight of her remark is especially true of the prenatal period during which critical phases of brain development are accomplished. Derangement of development of any region of the brain during this period is lifelong. *There is no catch-up later for missed or stunted development. Preterm delivery and low birthweight carry the highest risk of prenatal brain disorder and cerebral palsy.*

In order for you to understand our work it is important to remind you that the brain is a fatty substance made with highly specialised essential fats which you have to obtain from the food you eat. These essential fats form the membranes which enable cell specialisation, and specifically in the brain provide the functional structures for signalling messages. The integrity of the membrane is also critical for the rapidly growing blood vessels in the brain. Leakage or rupture due to an inadequate composition can lead to inflammation, blockage of blood flow and regional cell death with scarring leading to CP.

To understand the nutritional requirements, you need to recall that the brain evolved in the sea 400-500 million years ago, where the nutrients used to make it were entirely of marine origin. A pretty obvious point. What is less well known is that our brains today are still made of the same sea-derived stuff. Hence the reason why Bertie Wooster was regularly at pains to point out that Jeeves was so intelligent because he virtually lived on fish!

There is robust evidence for the role of these essential fats for brain development, which was confirmed at a joint consultation of FAO and WHO, 2008-2010.

Our recent work is being conducted at the Chelsea & Westminster Hospital, Imperial College, under the leadership of Professor Mark Johnson, head of Obstetrics and Gynaecology; Dr Enitan Ogundipe, who is in charge of neurodevelopmental assessment; Dr Yiqun Wang, who is in charge of the lipid science; and the Little Foundation PhD student AnnieBelle Sassine. Professor David Edwards and his team at St Thomas’s Hospital are responsible for the magnetic resonance images (MRI) of the brain around the time of birth

which tell us if there is any abnormality, or if supplements have had an effect on the development of various regions of the brain before birth.

We set out to test the hypothesis that supplementing mothers with DHA from recruitment at their first antenatal clinic (12 weeks pma) might influence brain development as objectively assessed by birth outcome and MRI of the brain after birth. We measured the red cell DHA and other fatty acids at recruitment and at birth in the mother and new-born.

The first result has been accepted for publication. It provided a stunning and unexpected result. The red cell membrane is actually a piece of tissue and its composition reflects what the tissues make of the mother's diet. It has a half-life of 120 days; hence its composition is a summation of several months beforehand. In a population of 296 mothers the red cell composition for a fatty acid – oleic acid – predicted with a confidence of 93% preterm delivery at 34 weeks and a confidence of 85% at 30 weeks. Hence this marker is also predicting risk.

The MRI data which is in preparation for publication showed some effect of the supplement on head size and on differences in regions of the brain such as the cortex in the boys, but not the girls.

There are two important conclusions: first, because of the long half-life of the red cell, the fatty acid marker is telling us that it is the condition of the mother in the months leading up to conception which is of over-riding importance to the completion of the pregnancy to full term. It did not matter whether the mother took a supplement or not, nor her condition during the pregnancy – it was the condition of the mother in biological preparation for conception that matters most, with a stunning 93% confidence level.

That Nature prepares in advance for pregnancy should not be surprising. It is after all a general principle. You would not crouch at the Olympic starting grid next to Usain Bolt without preparation. You would not even get in your motor car to go on a long trip without checking your oil, water, petrol and tyres. Unfortunately, about half the pregnancies coming to our hospital, Chelsea & Westminster, are unplanned. Yet creating a new life, a new person, is truly the most important event in a lifetime.

The second conclusion comes from the nature of the oleic acid marker. A rise in membrane oleic acid is itself a marker for deficiency of membrane (tissue) DHA and several other essential fatty acids of dietary origin required by the brain. Because these are brain-specific, this result implies that global inadequacy of the stuff you need for brain development is linked to the highest known risk for developmental brain disorders.

The relatively weak response of the supplement in the MRI findings is consistent with the supreme importance of what happens before conception. Moreover, an effect visible in the boys and not the girls is also consistent with an essential fat deficiency, as males are far more susceptible than females.

Confidence levels as high as 93% are very rare in biology and medicine. Hence, we have a serious marker for risk. We now need to refine that marker not just to general risk but to specific risks such as autism, ADHD, learning and behavioural pathology and cerebral palsy. *The specificity of the markers will point to cause, and hence prevention.*

Tied to nutrition, we will also need to investigate the role of the immune system in exacerbating or repairing prenatal damage. We wish to study 1,000 pregnancies for the bulk of these neurodevelopmental disorders, and secondly, one of some 50,000 to nail cerebral palsy itself. Imperial College is especially suited for this study as we have five teaching hospitals linked to our science facility.

The deliverables will be a recipe to ensure the security of membrane integrity, lack of which is, we believe, the cause of disorder. Different recipes may well be required for the different disorders; however, it is worth remembering that the people who diagnose these conditions now refer to a spectrum, e.g. autistic spectrum disorders or ADHD spectrum, etc. *Hence there will likely be a commonality.*

This programme is not just of importance for cerebral palsy, it is also *vital for understanding and dealing with the rise in mental ill health*, now the most costly burden of ill-health in the UK and the West. In summary, in 2007 the DoH estimated mental ill health to cost £77 billion, a cost greater than heart disease and cancer combined. People said the high cost was just new diagnostics. Repeat in 2010 put the cost at £105 billion. The Wellcome Trust had it at £113 billion in 2013. Simon House here has done an analysis of the cost, which is substantially greater as violence was not included. A continued rise will result in an unthinkable outcome for humanity.

A previous Europe-wide study conducted by Dr Martin Bax at Chelsea & Westminster Hospital examined MRI images of the brains of children with cerebral palsy. All cases of identifiable lesions in the brain were timed to well before the time of birth. This means they were not in the main due to obstetric mishap. As Professor Paul Polani at Guy's had previously concluded, there was no specific genetic cause, and that means the cause was environmental – i.e. nutrition and/or infection.

Just as we learnt how to prevent neural tube defects with folic acid, it is now on the cards that we can similarly make CP and its allied neurodevelopmental disorders and mental ill-health things of the past, with a knock-on ability to enhance the health and abilities of future children. It is the future of our children that is at stake."